



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification ⁴ : A61K 7/38</p>	<p>A1</p>	<p>(11) International Publication Number: WO 89/ 02264</p> <p>(43) International Publication Date: 23 March 1989 (23.03.89)</p>
<p>(21) International Application Number: PCT/DK88/00148</p> <p>(22) International Filing Date: 6 September 1988 (06.09.88)</p> <p>(31) Priority Application Number: 4835/87</p> <p>(32) Priority Date: 15 September 1987 (15.09.87)</p> <p>(33) Priority Country: DK</p> <p>(71) Applicant (for all designated States except US): CLAUS RIEMANN & CO. APS [DK/DK]; Malmbergsvej 3, DK-2850 Nærum (DK).</p> <p>(72) Inventor; and (75) Inventor/Applicant (for US only) : BAR-SHALOM, Daniel [IL/DK]; Rypevænget 213, DK-2980 Kokkedal (DK).</p> <p>(74) Agent: PLOUGMANN & VINGTOFT; Sankt Annæ Plads 11, DK-1250 København K (DK).</p>		<p>(81) Designated States: AT (European patent), AU, BE (European patent), CH (European patent), DE (European patent), DK, FR (European patent), GB (European patent), IT (European patent), JP, LU (European patent), NL (European patent), NO, SE (European patent), US.</p> <p>Published <i>With international search report.</i></p>
<p>(54) Title: ANTIPERSPIRANT COMPOSITION</p>		
<p>(57) Abstract</p> <p>An antiperspirant composition comprising $AlCl_3$ and one or more aluminium salts of one or more acids dissolved and/or dispersed in a suitable carrier, the acid or acids having no pK value in aqueous solution below 2.5, preferably not below 3, in particular not below 3.5, especially not below 4. The acid may preferably itself have antiperspirant, deodorant, astringent, antiseptic, antimicrobial, antifungal, or antiinflammatory properties and may in particular be selected from acetylsalicylic acid, salicylic acid, benzoic acid, propionic acid, octanoic acid, undecanoic acid, sorbic acid, ascorbic acid, lactic acid, malic acid, stearic acid, citric acid, phthalic acid, tartaric acid, or a naturally occurring amino acid. The antiperspirant composition causes significantly less or no irritation of the skin because the acid or acids, upon release from its aluminium salt, reacts with and removes the hydrochloric acid formed as a result of the reaction between $AlCl_3$ and the water in sweat.</p>		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	FR	France	ML	Mali
AU	Australia	GA	Gabon	MR	Mauritania
BB	Barbados	GB	United Kingdom	MW	Malawi
BE	Belgium	HU	Hungary	NL	Netherlands
BG	Bulgaria	IT	Italy	NO	Norway
BJ	Benin	JP	Japan	RO	Romania
BR	Brazil	KP	Democratic People's Republic of Korea	SD	Sudan
CF	Central African Republic	KR	Republic of Korea	SE	Sweden
CG	Congo	LI	Liechtenstein	SN	Senegal
CH	Switzerland	LK	Sri Lanka	SU	Soviet Union
CM	Cameroon	LU	Luxembourg	TD	Chad
DE	Germany, Federal Republic of	MC	Monaco	TG	Togo
DK	Denmark	MG	Madagascar	US	United States of America
FI	Finland				

ANTIPERSPIRANT COMPOSITION

FIELD OF THE INVENTION

The present invention relates to an antiperspirant composition as well as a method for controlling perspiration without the disadvantages often associated with such methods.

BACKGROUND OF THE INVENTION

It is a well known fact that AlCl_3 is a most effective antiperspirant salt (Høltze E., Kligman A.: "Mechanism of antiperspirant aluminium salts." *J. Soc. Cosmet. Chem.* 30, 279 (1979), and Shelley B., Hurley H.J.: "Studies on topical antiperspirant control of axillary hyperhidrosis." *Acta Dermatoven. Stockh.* 55, 241 (1975)). Most of the commercially available antiperspirant compositions contain AlCl_3 as the active component, e.g. dissolved in a suitable solvent. AlCl_3 exerts its antiperspirant activity by reacting with water to form aluminium hydroxychloride which acts as an astringent and thereby reduces the sweat output of the sweat glands. However, the disadvantage of using AlCl_3 is that the reaction with water to form aluminium hydroxychloride also generates hydrogen chloride or hydrochloric acid as a side product which may cause local skin irritation because of the high acidity; in most clinical studies, 20-50% of the members of the test groups indicated that irritation occurred, and about 10% reported severe irritation (soreness). Also, clothes in contact with the application area may be damaged, and both of these adverse effects can be ascribed to the formation of hydrochloric acid on the skin and in the sweat ducts.

Also, the antiperspirant activity of AlCl_3 is furthermore believed to be partly due to the aluminium hydroxychloride forming a perspiration-blocking "cast" of a polymeric gel precipitate in the sweat ducts. However, the acidity generated in sweat which reacts with AlCl_3 will impair the efficiency of the AlCl_3 -containing composition since AlCl_3 is not capable of forming the gel precipitate when the water with which it reacts has a pH of less than 5; among other

things this means that the AlCl_3 composition is not effective when used during sweating.

In the known art, several attempts have been made to prevent the development of acid which causes skin irritation and damaging of clothes. Thus, European Patent No. 70517 describes a two-part kit comprising an AlCl_3 -containing composition and a basic buffer composition, the basic composition being applied subsequent to the AlCl_3 -containing composition but after having allowed the AlCl_3 -containing composition to work for a certain specified period of time. However, as will be self-evident, such a two-stage application sequence is not very practical in actual use since most users would much prefer to have the antiperspirant treatment conducted in a single application.

From the above it is clear that there is a need for an antiperspirant composition which, while still having the advantages conferred by AlCl_3 , does not have the consequent disadvantages and which at the same time is simple to use.

SUMMARY OF THE INVENTION

The above described disadvantages in the known art are avoided in the antiperspirant composition of the invention which comprises AlCl_3 and one or more aluminium salts of one or more acids dissolved and/or dispersed in a suitable carrier, the acid or acids having no pK value in aqueous solution lower than 2.5 and being present in an amount capable of substantially neutralising the amount of hydrogen chloride formed by the hydrolysis of the amount of AlCl_3 present.

The idea behind the invention is to exploit the high acidity of hydrogen chloride by allowing the hydrogen chloride to react with a salt of the weaker acid with no pK value below 2.5, the weaker acid then, according to well known principles, being liberated from the salt by the stronger hydrochloric acid to give the free weaker acid and a chloride instead. The fact that an aluminium salt of the weaker acid is used has the advantage of resulting in the formation of a further amount of aluminium hydroxychloride, thereby resulting in a

further antiperspirant effect. On the other hand, the acidity is lowered considerably since the free acid present in the skin environment is now not solely hydrogen chloride. In effect the weaker acid with no pK value below 2.5, the aluminum salt of which forms part of the composition of the invention. Since the salt is less irritant to the skin, the net result is a reduction in or elimination of the skin irritation.

DETAILED DESCRIPTION OF THE INVENTION

- In order to prevent premature reaction of aluminum salts with water, it is preferred that the composition is anhydrous or in particular obtained by using a capillary system which is anhydrous or has no available water. Aluminum chloride does not undergo hydrolysis to aluminum hydroxide and hydrogen chloride. The term "no available water" is intended to mean that the water present in the form of moisture is not available to react with the aluminum salts, either because the water is present in too small an amount, or because the water is too strongly bound as a component in the composition. $AlCl_3$ will for example undergo no hydrolysis in 95% ethanol or in liquid sorbitol.
- A preferred composition is one in which the weaker acid/acids has/have no pK value below 3, in particular not below 3.5, especially not below 4. The use of an acid or acids with such properties will ensure a significant reduction in the level of skin irritation. The acid or acids is/are preferably physiologically acceptable.
- Since a number of organic acids have various biological properties, it is preferred that an acid in the composition of the invention has a biological effect such as astringent, antibacterial, antimicrobial, antiseptic, antifungal, antiparasitic, antiperspirant, deodorant, antiinflammatory, emollient, anesthetic, hemostatic, antipruritic properties, etc. By using an aluminium salt of one or more acids with one or more such properties, the properties of the composition of the invention may be amplified as well as expanded in its spectrum. Thus, if the acid used in the composition of the invention has antifungal properties, the composition of the invention could be useful in

therapy or prophylactic treatment of *Tinea pedis*, also known as "athlete's foot". This affliction is extremely common and is associated with sweating, and the maceration of the skin by the sweat facilitates the infection and makes it more difficult to treat. Even in persons with "normal" sweating it is desirable to reduce the amount of perspiration when treating the fungi.

Potentially useful acids with no pK value in aqueous solutions below 2.5 are the following: acetic, propionic, citric, acetylsalicylic, benzoic, salicylic, ascorbic, nicotinic, tartaric, phthalic, lactic, fatty acids (oleic, linoleic, undecenoic, octanoic, palmitic, ricinoleic, stearic, etc.), acetylchitosinic, succinic, carbamoylphenoxycetic, diacetylsalicylic, anthranilic, mefenamic, gentisic, tolfenamic, acetotartaric, agaric, formic, subacetic, ellagic, fumaric, malic, morrhuaic, oxalic, para-amino-benzoic, gallic, cinnamic, isoascorbic, sorbic, aminocaproic, aminomethylbenzoic, tranxenamic acid, naturally occurring amino acids such as glycine, alanine, valine, leucine, isoleucine, serine or threonine, etc. and derivatives thereof as well as tar acids, phenol, thymol and cation exchange resins. The term "derivatives thereof" is intended to mean that the various acids listed may also be further substituted with various groups, the presence of derivative substituents conferring one or more of the biological properties mentioned above to the acid in question. The substituent groups forming the derivatives may be selected from a broad range such as phenyl, phenylamino, naphthyl, benzoyl, indenyl or various heterocyclic groups such as indolyl, benzoxazolyl, pyridyl, benzindolyl etc., the substituent groups optionally themselves being substituted with substituents such as halogen, alkyl, alkoxy, optionally alkylsubstituted amino etc.

Thus, various derivatives of propionic, acetic, phenylacetic, salicylic, and anthranilic acid etc. are able to inhibit prostaglandin synthesis and can therefore function as local antiinflammatory agents. Examples of propionic acid derivatives are naproxen, ibuprofen, benoxaprofen, and buclixic acid; examples of phenylacetic and acetic acid derivatives are indomethacin, bufexamac, diclofenac, sulindac, and aclofenac; examples of salicylic acid derivatives are aspirin, acetaminosalol, diflunisal, dipyracetyl, and fendal; exam-

ples of anthranilic acid are etofenamic acid, flufenamic acid, meclofenamic acid, and tolfenamic acid; and an example of butyric acid derivatives is fenbufen.

Among the acids listed above, several are known to have some of the biological properties mentioned above. Thus, salicylic, acetotartaric, agaric, formic, subacetic and ellagic acid are known to have astringent properties, and undecenoic, octanoic, propionic, tolfenamic, isoascorbic and sorbic acid are known to have antifungal properties.

Preferred examples of acids having no pK value below 2.5 are acetylsalicylic, salicylic, benzoic, propionic, octanoic, undecanoic, sorbic acid, ascorbic acid, lactic acid, malic acid, stearic acid, citric acid, phthalic acid, tartaric acid, or a naturally occurring amino acid.

In order to ensure satisfactory neutralization of any hydrogen chloride liberated as a result of the reaction between $AlCl_3$ and water, the molar ratio between the aluminium salt or salts of the acid or acids and $AlCl_3$ is preferably in the range from 1:1 to 1:2, in particular about 2:3.

In order to provide a composition effective for antiperspirant purposes, it is preferred that the $AlCl_3$ and the aluminium salt of the acid is present in the composition of the invention in amounts corresponding to a total aluminium content of up to 3 gram atoms of Al per kilogram of composition, in particular from 1.0 to 2.0 gram atoms Al per kg composition.

The carrier or carriers in which the $AlCl_3$ and the aluminium salt of the weaker acid is dissolved and/or dispersed may be any of the carriers traditionally used for incorporation into antiperspirant compositions. Thus, the carrier may be a liquid, a gel, a semisolid or a powder. Liquid carriers may be alcohols, glycols, fats, fatty acid esters, fatty acids, paraffins, liquid polymers (such as silicone oil), for example ethyl alcohol, isopropyl myristate, glycerine, propylene glycol, etc. as well as mixtures thereof. A gel carrier may

be an alcohol or another of the above mentioned liquid carriers such as ethyl alcohol containing a cellulose derivative such as hydroxypropyl cellulose. A semisolid carrier may be a polyglycol, a paraffin (for example vaseline), fats, or any of the above mentioned liquids
5 containing a polymer such as liquid paraffin containing dissolved polyethylene (marketed under the trade name Plastibase). A solid carrier may be talc, starch, kaolin etc.

The invention further relates to a method for controlling perspiration comprising applying to a skin area where perspiration is to be
10 controlled an antiperspirant composition as described above.

The composition of the invention may be prepared by methods commonly used within the art for the preparation of antiperspirant compositions, the preparation ordinarily comprising simply mixing together the constituents. Thus, a liquid composition may be prepared by dis-
15 solving or dispersing the aluminium chloride and the weaker acid/acids in the liquid carrier; optionally, the aluminium chloride and the weaker acid/acids may be dissolved or dispersed separately in two portions of the carrier or in two different carrier components followed by mixing of the mixtures. A gel composition may be obtained
20 by starting from a liquid composition and adding gelling agent such as the above mentioned cellulose derivative.

The invention is further illustrated by the following non-limiting examples.

EXAMPLE 1

25 An antiperspirant composition was prepared from the following ingredients:

Aluminium chloride	10.0 g
Aluminium hydroxydisalicylate	12.5 g
Isopropyl myristate	10.0 ml
30 Absolute ethanol q.s.	100.0 ml

The aluminium chloride was dissolved in about 50 ml absolute ethanol to form a solution. The aluminium hydroxydisalicylate was dispersed thoroughly in the isopropyl myristate, and to the resulting dispersion, the aluminium chloride solution was added while stirring to give an antiperspirant composition comprising a dispersion of aluminium hydroxydisalicylate in a liquid medium comprising aluminium chloride, isopropyl myristate, and absolute ethanol.

TEST

The composition prepared above (composition II) was tested by comparison with a classical type antiperspirant consisting of a 20% w/w solution of aluminium chloride in absolute ethanol (composition I). Ten volunteers applied composition I to their left armpit and composition II to their right armpit for 10 days. Thereafter, the application pattern was switched around so that composition I was applied to the right armpit and composition II to the left, the application again being continued for 10 days. Eight out of the ten persons reported some kind of irritation in the armpit to which composition I was applied, whereas only one person on two of the total of twenty test days reported some irritation in the armpit when using composition II. The antiperspirant effects of the two compositions were the same.

EXAMPLE 2

Other compositions according to the invention comprise:

A:	Aluminium chloride	10.0 g
25	Aluminium hydroxydibenzoate	10.0 g
	Aluminium hydroxydisalicylate	5.0 g
	Isopropyl myristate	8.0 ml
	Absolute ethanol q.s.	100.0 ml

B:	Aluminium chloride	10.0 g
30	Aluminium hydroxydibenzoate	8.0 g
	Aluminium hydroxydisalicylate	4.0 g

Aluminium hydroxydiundecan ate	3.0 g
Excipient q.s.	100.0 g

The excipient in composition B may be e.g. talc giving a solid composition.

5 EXAMPLE 3

Antiperspirant ointment

An antiperspirant ointment was prepared from the following ingredients:

	Polyethylen glycol 3000	175.0 g
10	Polyethylen glycol 400	175.0 g
	25% solution of $AlCl_3$ in absolute ethanol	750.0 g
	Aluminium hydroxydilactate	120.0 g
	Absolute ethanol	160.0 g

- 15 The polyethylen glycols were mixed in a melt whereupon the remaining ingredients were mixed into the melt in a high-shear homogenizer resulting in an ointment upon cooling.

EXAMPLE 4

Antiperspirant stick

- 20 An antiperspirant stick was prepared from the following ingredients:

	Aluminium tristearate	11.0 g
	Polyethylene glycol 6000	10.0 g
	Stearyl alcohol	10.0 g
	Polyethylene glycol 400	
25	monostearate	10.0 g
	Aerosil (very fine silica)	2.0 g
	25% solution of $AlCl_3$ in absolute ethanol	40.0 g

Aluminium hydroxydilactate	10.0 g
Absolute ethanol q.s.	to 100.0 g


- Aluminium stearate, polyethylene, glycol 6000, stearyl alcohol and polyethylene glycol 400 monostearate were mixed by melting the
- 5 ingredients together. Thereafter, aerosil, ethanol and AlCl_3 -solution in ethanol was added and mixed followed by addition and mixing of aluminium hydroxydilactate. Finally, the mixture was cooled in a mould giving an antiperspirant stick.

CLAIMS

1. An antiperspirant composition comprising AlCl_3 and one or more aluminium salts of one or more organic acids dissolved and/or dispersed in a suitable carrier, said acid or acids having no pK value
5 in aqueous solution lower than 2.5 and being present in an amount capable of substantially neutralising the amount of hydrogen chloride formed by the hydrolysis of the amount of AlCl_3 present.
2. An antiperspirant composition as claimed in claim 1 in which the carrier is anhydrous or has no available water for the hydrolysis of
10 AlCl_3 .
3. A composition as claimed in claim 1 or 2 in which the acid or acids has/have no pK value below 3.
4. A composition as claimed in claim 3 in which the acid or acids has/have no pK value below 3.5.
- 15 5. A composition as claimed in claim 4 in which the acid or acids has/have no pK value below 4.
6. A composition as claimed in any of claims 1-5 in which the acid or acids has/have antiperspirant, deodorant, astringent, antiseptic, antimicrobial, antifungal, or antiinflammatory properties.
- 20 7. A composition as claimed in any of claims 1-6 in which the acid or acids is/are selected from acetylsalicylic acid, salicylic acid, benzoic acid, propionic acid, octanoic acid, undecanoic acid, sorbic acid, ascorbic acid, lactic acid, malic acid, stearic acid, citric acid, phthalic acid, tartaric acid, or a naturally occurring amino
25 acid.
8. A composition as claimed in any of the previous claims in which the molar ratio between the aluminium salt or salts of the acid or acids and AlCl_3 is in the range from 1:1 to 1:2.

INTERNATIONAL SEARCH REPORT

International Application No PCT/DK88/00148

I. CLASSIFICATION F SUBJECT MATTER (if several classification symbols apply, indicate all) ⁶		
According to International Patent Classification (IPC) or to both National Classification and IPC 4		
A 61 K 7/38		
II. FIELDS SEARCHED		
Minimum Documentation Searched ⁷		
Classification System	Classification Symbols	
IPC	A 61 K 7/00, 7/32, 7/38	
US Cl.	424:46, 47, 65-68	
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched ⁸		
SE, NO, DK, FI classes as above		
III. DOCUMENTS CONSIDERED TO BE RELEVANT⁹		
Category ¹⁰	Citation of Document, ¹¹ with Indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
X	US, A, 2 087 161 (WILLIAM C. MOORE) 13 July 1937	1-12
Y	SE, B, 365 115 (THE J.B. WILLIAMS COMPANY INC.) 18 March 1974	1-12
Y	DE, A1, 2 423 637 (SOBEL, JACK) 27 November 1975	1-12
<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p>¹⁰ Special categories of cited documents:</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 45%;"> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</p> <p>"A" document member of the same patent family</p> </div> </div>		
IV. CERTIFICATION		
Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report	
1988-12-13	1988 -12- 21	
International Searching Authority	Signature of Authorized Officer	
Swedish Patent Office	 Elisabeth Carlborg	